

SYPHILIS

I. INTRODUCTION

Syphilis is a chronic, systemic disease caused by a spirochete, *Treponema pallidum*. Despite availability of sensitive diagnostic tests and effective treatment, it remains a serious health problem. Syphilis has two routes of transmission:

- (1) sexual transmission, which accounts for the vast majority of cases, and
- (2) vertical transmission from mother to fetus in utero.

Congenital syphilis can lead to stillbirth, prematurity and to a variety of clinical complications including central nervous system damage.

Sexual transmission occurs through exposure to *Treponema pallidum* present in open lesions of infected individuals. The majority of new reported cases of syphilis are in men who have sex with men, but rates of infection among women of reproductive age as well as cases of congenital syphilis have risen in the last decade.

II. PROGRESSION OF SYPHILIS INFECTION

- A. Infection and incubation: Exposure to *Treponema pallidum* from an open lesion in an infected individual can lead to infection in nearly any site/tissue that comes in contact with infected secretions. Following inoculation, there is an incubation period that varies from 10 to 90 days (average about three weeks) before primary syphilis is apparent.
- B. Primary Syphilis: Primary syphilis is characterized by a painless lesion at the site of inoculation. This primary lesion is often missed. Systemic dissemination of the spirochete quickly follows.
- C. Secondary Syphilis: Weeks to a few months later, approximately 25 percent of individuals with untreated infection develop secondary syphilis, a systemic illness characterized by a disseminated rash (a distinguishing characteristic of which is sores on the palms of the hands and soles of the feet), fever, headache, malaise and diffuse lymphadenopathy. Secondary syphilis is usually self-resolving.
- D. Latent Syphilis: The period of time when an individual is asymptomatic, but has antibody titers consistent with infection is known as latent syphilis.
- E. Late or Tertiary Syphilis: In untreated clients, syphilis infection may progress to late disease with manifestation of central nervous system involvement (neurosyphilis), cardiovascular syphilis, gummatous syphilis (granulomatous, nodular lesions which can occur in a variety of organs) and other clinical manifestations.

III. HISTORY AND EVALUATION

- A. History may include:
 1. History of other STI
 2. Recent change in sexual partner
 3. Partner with symptoms of syphilis

4. Lack of STI protection (condom use)
5. Report of multiple sexual partners
6. Report of illicit drug use
7. Recent incarceration
8. Reports of engaging in commercial sex work
9. Infected partner
- B. Symptoms may include:
 1. In Primary Syphilis:
 - a. Painless, one to two centimeter lesion
 - b. Swollen lymph nodes
 2. In Secondary Syphilis:
 - a. Rash of trunk and extremities including soles of feet and palms of hands
 - b. Systemic symptoms: fever, headache, malaise, anorexia, sore throat, myalgias, and weight loss
 - c. Hair loss
 - d. Visual changes
- C. Physical exam findings may include:
 1. In Primary Syphilis:
 - a. Chancre of primary syphilis, a one to two centimeter ulcer with a raised, indurated margin
 2. In Secondary Syphilis:
 - a. Non-vesicular rash of the trunk and extremities with involvement of palms and soles
 - b. Lymphadenopathy
 - c. Condyloma lata – large, raised white or gray lesions in moist warm areas including mucous membranes
 - d. Hepatic and renal lab abnormalities
 - e. Abnormal neurologic exam

IV. SCREENING AND DIAGNOSIS

- A. Any client who attends family planning clinic should be offered nontreponemal serologic screening for syphilis annually if they are at risk and especially if they meet any one of the following criteria:
 1. Persons with a sexually transmitted disease within the last year, including HIV
 2. Persons participating in exchange of sex for drugs or money or partners of persons participating in exchange of sex for drugs or money
 3. Persons participating in illicit drug use or partners of persons participating in illicit drug use
 4. History of admittance to jail or other detention facility or partner of person that has been in jail or other detention facility
 5. Sex with partner with high-risk behavior, including men having sex with men
 6. Sex with partner diagnosed with active syphilis.
 7. Women exposed to syphilis through an infected partner should be tested and treated presumptively.
 8. Any skin lesions suggesting syphilis (clients with suspicious lesions should be evaluated promptly).

- B. Screening in pregnant women is recommended to prevent in utero transmission of asymptomatic infection, which can lead to congenital syphilis.
- C. Testing for syphilis can occur in two manners:
 - 1. Serologic testing:
 - a. Nontreponemal tests (non-specific, used for primary screening)
 - i. Venereal Disease Research Laboratory (VDRL)
 - ii. Rapid Plasma Reagin (RPR)
 - iii. Tolidine Red Unheated Serum Test (TRUST)
 - b. Treponemal tests: (usually done to confirm infection).
 - i. Treponemal antibody test (FTA)
 - 2. Direct testing from clinical specimens:
 - a. Darkfield microscopy
 - b. Direct fluorescent antibody (DFA)
 - c. Polymerase chain reaction (PCR) testing methods (investigational)
- D. While direct identification of *T. pallidum* by either darkfield microscopy or DFA represents a definitive diagnosis of syphilis, due to the difficulties inherent in this type of testing, the mainstay of syphilis testing is serologic testing, which combined with history and symptoms that provides a presumptive diagnosis.
- E. A positive nontreponemal serologic test (VDRL or RPR) should be followed immediately with a treponemal antibody serologic test (FTA) to confirm the diagnosis of syphilis.
- F. If the RPR or VDRL serologic test for syphilis is reactive, but the FTA is non-reactive, and there is no clinical evidence of syphilis, treatment is not indicated. In this instance, both tests should be repeated within 4 weeks.
- G. The nontreponemal tests may yield false-positive results in individuals who recently experienced an acute febrile illness, recent immunization, or are pregnant. Persistent false-positive results are seen in individuals with chronic infections, autoimmune disease, or narcotic addiction. The titers are usually less than 1:8.
- H. Treponemal antibody test (FTA), once positive usually remains so for life regardless of the treatment or disease activity.
- I. Nontreponemal antibody titers (VDRL or RPR) tend to correlate with disease activity. A high titer (>1:16) usually indicates disease. A fourfold change in titer, equivalent to a change of two dilutions (e.g., from 1:16–1:4 or from 1:8–1:32), is considered necessary to demonstrate a clinically significant difference between two nontreponemal test results that were obtained using the same serologic test.
- J. Sequential serologic tests in individual clients should be performed by using the same testing method (e.g., VDRL or RPR), preferably by the same laboratory.

V. TREATMENT

- A. Clients with a positive test result (positive treponemal plus positive nontreponemal serologic test OR diagnosis via direct method) or clients with symptoms and sexual contact with confirmed positive partner should be treated immediately following the most recent CDC Sexually Transmitted Diseases Treatment Guidelines which can be accessed at CDC website: <https://www.cdc.gov/std/tg2015/syphilis.htm>
- B. Clients for whom there is documented evidence of adequate treatment of syphilis in the past need not be retreated unless there was insufficient follow-up or there

- is clinical or serologic evidence of reinfection (e.g., a four-fold titer rise in a quantitative nontreponemal test). Call STD Control at DHMH at 410-767-6690 to check on previous titers, if necessary.
- C. Treatment of the client's sexual partner is an important part of the therapeutic regimen. The partner should be referred for treatment and evaluation for other reproductive tract infections.
 - D. The time periods before treatment used for identifying at-risk sexual partners are
 1. 3 months plus duration of symptoms for primary syphilis,
 2. 6 months plus duration of symptoms for secondary syphilis, and
 3. 1 year for early latent syphilis.
 - E. All clients with syphilis should be offered counseling and testing for HIV infection.

VI. SPECIAL TREATMENT CONSIDERATIONS

- A. Penicillin allergies: parenteral benzathine penicillin G is the recommended treatment for syphilis. There are alternative regimens, but clients who are allergic to penicillin and are pregnant, HIV-infected, have evidence of tertiary syphilis or neurosyphilis require desensitization and treatment with penicillin.
- B. Desensitization is also recommended for treatment of clients with early latent syphilis in whom follow-up would be difficult.
- C. Treatment of penicillin allergic clients should be conducted in collaboration with specialists in obstetrics (for pregnant clients) or infectious diseases specialists (for non-pregnant clients).

VII. FOLLOW-UP

- A. Quantitative nontreponemal serologic test should be repeated at the following intervals: 6, 12, and 24 months.
- B. If titers increase four-fold, if an initially high titer ($>1:32$) fails to decrease, or if the client has signs or symptoms attributable to syphilis, the client should be evaluated for neurosyphilis and treated appropriately.
- C. To prevent congenital syphilis and other pregnancy complications related to syphilis and to treatment of syphilis, coordinated prenatal care and treatment is essential. Pregnant women diagnosed with syphilis need to be referred immediately for prenatal care with prenatal care provider able to appropriately treat and manage syphilis in pregnancy.

VIII. REPORTING

Maryland law requires provider and laboratory reporting of all cases of syphilis. Reporting instructions and forms can be accessed via the Maryland DHMH Infectious Disease and Environmental Health Administration (IDEHA) website:
<http://phpa.dhmv.maryland.gov/Pages/what-to-report.aspx>

REFERENCES

CDC: Sexually Transmitted Disease Treatment Guidelines, 2015